

## **Lecture 3**

### **Krebs cycle**

### **Metabolic disorder of Carbohydrate Metabolism**

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## **CITRIC ACID CYCLE**

Tricarboxylic acid cycle, (TCA cycle), also called Krebs cycle and citric acid cycle, the second stage of cellular respiration.

### **- What is TCA cycle?**

TCA cycle is the final common pathway for metabolism of carbohydrates, lipids, and proteins (III Phase of metabolism). It is a cyclic process, and involves a sequence of compounds interrelated by oxidation-reduction and other reactions which finally produces CO<sub>2</sub> and H<sub>2</sub>O.

### **- Why TCA cycle is also called Krebs cycle or citric acid cycle?**

Krebs first discovered this cycle hence also called as “Krebs cycle”.

First compound formed by combination of OAA and acetyl CoA is citric acid, hence called as citric acid cycle.

### **- Where and under what conditions does TCA cycle function?**

Mitochondria of the cells. • Under aerobic conditions-requires presence of O<sub>2</sub>.

### **- Can TCA cycle function in absence of O<sub>2</sub>?**

TCA cycle cannot function in absence of O<sub>2</sub>.

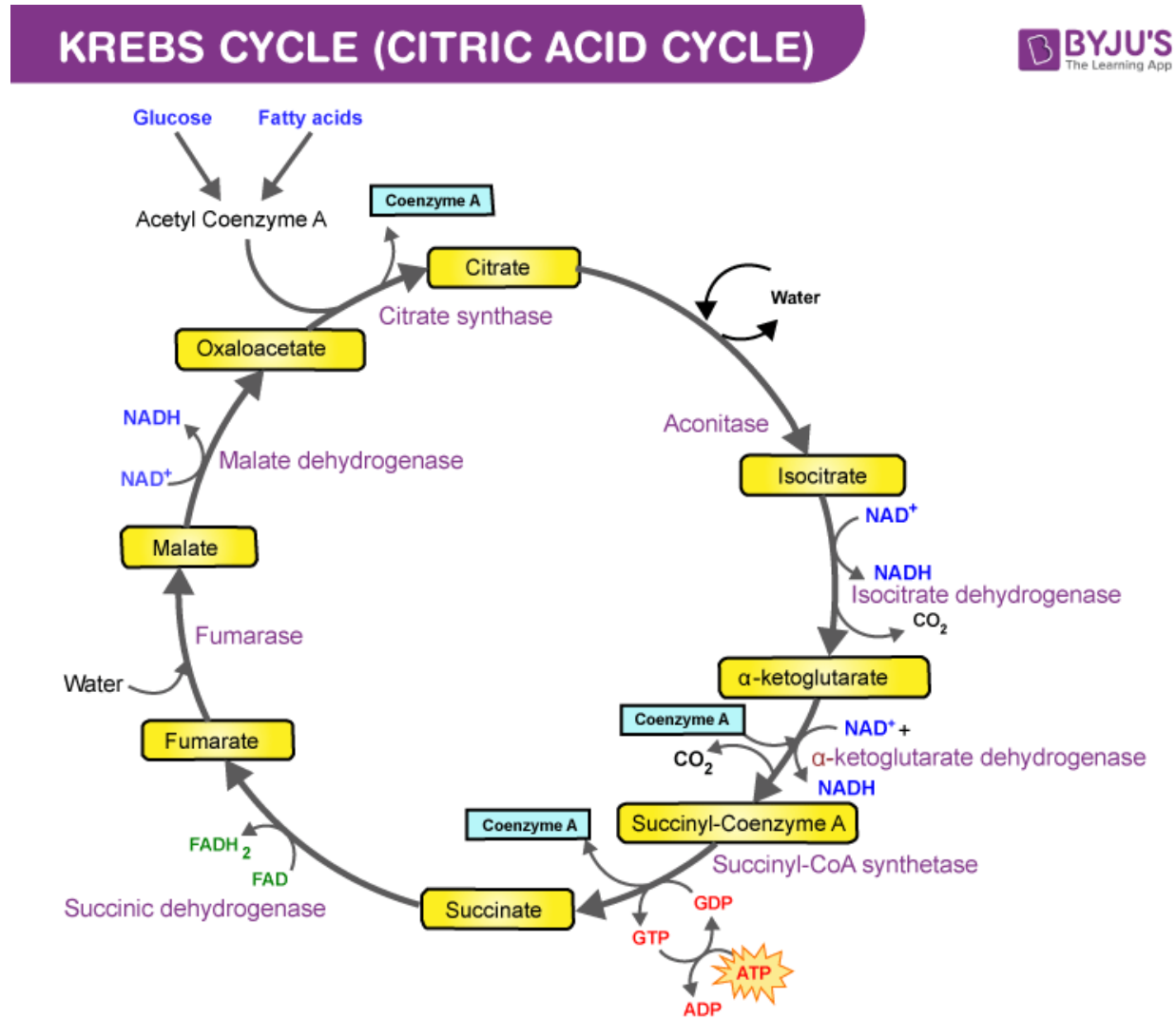
### **Where are the enzymes of TCA cycle located?**

Enzymes of TCA cycle are located in mitochondrial matrix, either free or attached to the inner surface of the inner mitochondrial membrane, which facilitates the transfer of reducing equivalents to the adjacent enzymes of ETC.

### **The steps include in the citric acid cycle are:**

1. Formation of Citrate
2. Formation of Isocitrate via cis-Aconitate
3. Oxidation of Isocitrate to α-Ketoglutarate and CO<sub>2</sub>
4. Oxidation of α-Ketoglutarate to Succinyl-CoA and CO<sub>2</sub>

5. Oxidation of Succinate to Fumarate
6. Hydration of Fumarate to Malate
7. Oxidation of Malate to Oxaloacetate



**Figure(1):Citric acid cycle**

### Diabetes mellitus (DM)

Definition: - is a systemic metabolic disorder characterized by hyperglycemia and abnormal insulin production and /or action. Insulin is a hormone produced by the pancreas. it controls the level of glucose in the blood by regulating the production and storage of glucose.

-Beta cells are responsible for production and secreting insulin and glucagons.

-It is anabolic or storage hormone. When a meal is eaten, insulin secretion increases and moves glucose from the blood into the muscle, liver, and fat cell.

**In those cells insulin has the following effect.**

o Stimulate storage of glucose in the liver and muscle

o Enhance storage of dietary fat in the adipose tissue

o Accelerate transport of amino acid in to the cells .

- glucagons are an essential factor in the development of DM. It increases blood glucose concentrations .

**Classification of diabetes**

Type 1-IDDM Type 2-NIDDM Other specific subtype- like malnutrition related Diabetic Mellitus (MRDM), gestational DM

1- Type 1 DM - Is characterized by destruction of the pancreatic beta cells - The exact cause is unknown hat a combination of Genetic , Environmental factors that contribute to beta cell destruction and Genes regulating immune response are involved

2- Type 2 DM - Is related to insulin resistance (a decreased sensitivity to insulin) and impaired insulin secretion .

**Risk factors include:**

1- Age (insulin resistance tends to increase with age over 65)

2- Obesity

3- Family history is strongly associated or environmental factors, e.g. Viruses

4- Diagnostic Criteria for Diabetic Mellitus Fasting plasma glucose (FPG) >126mg/dl Random blood glucose (RBS) >200mg/dl with symptoms 2hr post load glucose >200mg/dl .

**There are four components of management for diabetes:** - Diet - Exercise , Monitoring blood glucose , Medication (as needed) .

### **Symptoms of high blood sugar include**

Frequent urination, increased thirst, and increased hunger. If left untreated, diabetes can cause many complications. Acute complications can include diabetic ketoacidosis, hyperosmolar hyperglycemic state, or death, Serious long-term complications include cardiovascular disease, stroke, chronic kidney disease, foot ulcers, and damage to the eyes Diabetes is due to either the pancreas not producing enough insulin, or the cells of the body not responding properly to the insulin produced.

### **Diabetic ketoacidosis (DKA)**

- o Life-threatening complication of Type 1 DM
- o Occurs in the absence of insulin
- o Results in metabolic acidosis

-Type 2 diabetes begins with insulin resistance, a condition in which

cells fail to respond to insulin properly. As the disease progresses, a lack of insulin may also develop. This form was previously referred to as "non - insulin-dependent diabetes mellitus" (NIDDM) or "adult-onset diabetes".

The most common cause is a combination of excessive body weight and insufficient exercise.

- Accounts for 90% of patients with diabetes
- Usually occurs in people over 40 years old
- 80-90% of patients are overweight

### **Insulin resistance**

- o Body tissues do not respond to insulin
- o Results in hyperglycemia

- Gestational diabetes is the third main form, and occurs when pregnant women without a previous history of diabetes develop high blood sugar levels.

- Develops during pregnancy
- Detected at 24 to 28 weeks of gestation

**Associated with risk for cesarean delivery, perinatal death, and neonatal complications.**

### **Signs and symptoms**

The classic symptoms of untreated diabetes are 'weight loss, polyuria (increased urination), polydipsia (increased thirst), and polyphagia (increased hunger). Symptoms may develop rapidly (weeks or months) in type 1 diabetes, while they usually develop much more slowly and may be subtle or absent in type 2 diabetes.

### **COMPLICATIONS OF DIABETES MELLITUS**

May be classified into acute and chronic complications

- Acute complications are Diabetic ketoacidosis, Nonketotic ,hyperosmolar state Hypoglycemia
- Chronic complications , Affect many organ systems

**The vascular complications are further subdivided into**

**- Microvascular complications that includes**

- Diabetic retinopathy
- Diabetic nephropathy
- Diabetic neuropathy

**- Macrovascular complications**

1- Coronary artery disease 2- Peripheral vascular disease 3- Cerebrovascular Disease.